Journal of Palliative Care & Medicine
ISSN: 2165-7386

Couitchere et al., J Palliat Care Med 2019, 9:2
DOI: 10.4172/2165-7386.1000353

Review Article Open Access

Audit of Deaths in a Pediatric Oncology Unit in Sub-Saharan Africa

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Received date: January 15, 2019; **Accepted date**: January 23, 2019; **Published date**: March 1, 2019

Abstract

Introduction: There are few data on the mortality of children hospitalized for cancer in Sub-Saharan Africa. Reported death rates are usually high. This study describes the causes of death from childhood cancer.

Methods: This is an observational and descriptive study of the clinical and therapeutic characteristics of children (0-14 years) who died in the pediatric oncology unit of the University Hospital Center of Treichville in Abidjan from January 2010 to December 2015. Identified causes of death are reported.

Results: During this six year period, 249 inpatient children out of 681 died, resulting in a mortality rate of 36.5%, the median age of the deceased children was 6 years 10 months. Of the 139 who died in hospital, 131 were solid tumors and 48 were metastatic or at advanced stages in the Toronto classification. Of the 71 cases treated, 14 had received first-line palliative treatment. Treatment-related deaths accounted for 29.5% of cases and non-treatment-related deaths for 70.5%. The main causes of death were: tumor progression (42.5%), febrile aplasia (15.1%) and metabolic disorders (7.9%).

Conclusion: Actions promoting/ early diagnosis and treatment as well as improved supportive care will reduce mortality.

Keywords: Pediatric oncology; Death; Sub-saharan Africa

Introduction

In high-income countries, about 20% of children with cancer die, and cancer is the second leading cause of death in children [1,2]. This rate remains stable, paving the way for clinical research to identify new therapeutic alternatives. The reported death rates are in the order of 80% in low-income and middle-income countries [1,3]. African publications on the mortality of children with cancer are rare [4,5]. In the pediatric oncology unit of the University Hospital of Treichville in Abidjan, the overall survival of children with cancer reported in a population of 331 cases recruited from 1995 to 2004 was 9.4% and the death rate during the study period was 39,3% [6]. We performed an audit to identify the causes of deaths of hospitalized children and to improve patient survival in the pediatric oncology unit.

Methods

Our center is a referral oncology center with medical and surgical oncology. All services regularly treat patients on inpatient basis. Approximately 200 new pediatric cancer patients are seen annually and common cancers are lymphomas, leukemia, retinoblastoma and Wilms tumor.

This observational and descriptive study concerned children aged 0 to 14 years diagnosed with cancer (treated or non-treated with specific treatment) and having died in the oncology unit of the pediatric ward of the University Hospital of Treichville from January 1, 2010 to December 31, 2015. This unit is member of the GFAOP network. The collection of information for each death was based on data from the hospital register and the patient's medical file.

Cancer stages were established using Toronto guidelines [7]. Sociodemographic, clinical and therapeutic variables, delays (diagnosis, treatment) and causes of death were analyzed. The diagnostic delay was the time elapsed between the first symptoms and the diagnosis. The treatment delay was the time taken to initiate treatment after diagnosis. Deaths occurring within 90 days of anticancer therapy without tumor progression were considered as treatment-related mortality. Status of cancer at the time of death was recorded for all deaths.

Controlled cancer in solid tumors was defined as clinical and radiological absence of disease for at least 1 month; for hematological malignancies, besides clinical and radiological response, hematological

response was also considered to document the same. Non-responders and partial responders were grouped into uncontrolled malignancies. The cause of death was determined from the source documents, and the immediate cause mentioned was taken into account for the analysis. The cause of death, when not mentioned, was deduced from the clinical and paraclinical data of the last two weeks of life.

Statistical analysis was performed using the SPSS 15.0 software (SPSS Inc., Chicago, IL, USA), and included a description of the demographic and clinical parameters. The confidentiality rules of the International Agency for Research on Cancer (IARC 2004/03) were applied. This work was done with the agreement of the scientific director of the hospital.

Results

Six hundred and eighty-one patients were admitted during the study period, including 249 deaths, resulting in a mortality rate of 36.5%. This study included 139 files, 126 files had a diagnosis at the time of death.

Thirteen patients with clinical and radiological signs of cancer died before performing the histological examination. The basic characteristics of the study population are presented in Table 1.

Characteristics	N (%)
Age	139
0–4	41 (29.5)
5–9	60 (43.2)
10–14	38 (27.3)
Average	7 years
Median	6 years and 10 months
Extremes	(3 months–14 years and 4 months)
Gender	139
Male	87 (62.5)
Female	52 (37.5)
Sex ratio	1.6
Type of malignancies	139
Solids tumors	131 (94.2)
Leukemia	8 (5.8)
Diagnostic delay	126
Average	114 days
Median	90 days
Extremes	(15 days–720 days)

Table1: Baseline characteristics of the 139 cases.

The median age of the children who died was 6 years 10 months and the sex ratio was 1.6. The majority of deaths were in the 5-9 year age group (60=43.2%).

Metastatic or advanced-stage patients at diagnosis accounted for 38.1% of causes, and those with regional extension for 9.5% of cases (Table 2).

Main cancers	N (%)	Stages at death according to the Toronto classification (n)
Non-Hodgkin Lymphoma	70 (55.5)	Limited 46
		Advanced 23
		Unknown 1
Retinoblastoma	17 (13.5)	Localized 1
		Regional 11
		Metastatic 5
Acute Leukemia	8 (6.4)	CNS–4
		CNS+1
		Unknown 3
Sarcoma	10 (7.9)	Localized 3
		Metastatic 7
Wilms Tumor	7 (5.5)	Localized 4
		Metastatic 3
Neuroblastoma	6 (4.8)	Locoregional 1
		Metastatic 4
		Unknown 1
Germ cell tumors	3 (2.4)	Metastatic 3
Hodgkin's Lymphoma	2 (1.6)	3A 1
		4A 1
Others[1]	3 (2,4)	Localized 1
		metastatic1
		Unknown 1
Total	126 (100)	Localized/Limited/3A/CNS-: 60 (47.6%)
		Regional/Locoregional: 12 (9.5%)
		Metastatic/Advanced/4A/CNS +: 48 (38.1%)
		Unknown: 6 (4.8%)
Note: 1. Glioma (1), hepatoblastoma (1), melanoma (1)		

Table 2: Distribution of cancers and stratification (n=126).

Thirty-seven out of the 46 stage-limited lymphomas in the Toronto classification were diffuse abdominal forms. Several deaths occurred before or in less than 30 days after initiation of treatment (98 cases).

Sixty-eight deaths occurred in patients not treated. Of these, 13 died before performing the histological examination, 19 during nutritional rehabilitation and treatment of associated infections.

Twelve children had died just before the initiation of cancer treatment. Seventeen patients waiting for a blood transfusion died in

an acute anemia chart. The circumstances of death were not specific for the remaining eight cases.

The number of children treated was 71 (Table 3).

Characteristics	**N (%)**
Treatment of Patients	139
Treated patients	71 (51)
Untreated patients	68 (49)
For patients treated	71
Intent of therapy	
Palliative	14
Curative	57
Treatment delay	
Average	14 Days
Median	6 Days
Extreme	1 Day–130 Days
Deaths during the first 30 days of chemotherapy	
Yes	33 (46.5)
No	38 (53.5)
Time of onset of deaths compared with the start of chemotherapy	
Average	91 Days
Median	34 Days
Extreme	1 day–600 days
Status of patient at death	
Controlled disease	08 (11.3%)
Uncontrolled disease	63 (88.7%)

Table 3: Therapeutic characteristics of treated patients.

The average time to death from admission was 78 days and the median was 28 days (range: 1 day to 630 days). For patients who received treatment for curative purposes, the rhythm of administration of chemotherapy was irregular in 41 cases out of 57, with an average delay of 11 days during the inter-cure period (range: 3 days-51 days) and a median 7 days. The status of malignancy was controlled in 8/139 (5.7%) including 1 case of leukemia and 7 solid tumors. The one case of leukemia in complete remission died of severe anemia following a digestive hemorrhage.

Of 139 deaths, 41 (29.5%) occurred within 90 days of anticancer treatment of which 38 occurred after chemotherapy. Non-treatment-related deaths accounted for 70.5% (98 deaths).The main causes of death identified were tumor progression (42, 5%), febrile aplasia (15,1%) and metabolic disorders (7,9%) (Table 4).

Causes of death	**Lymphomas (n=72)**		**Neuroblastoma (n=6)**		**Wilms tumor (n=6)**		**Retinoblastoma (n=17)**		**Acute Leukemia (n=8)**		**Sarcomas (n=10)**		**Others* (n=7)**		**Undiagnosed Cancers (n=13)**		**Total (N=139)**	
	n	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
Tumor progression	20	27.8	4	66.6	4	66.6	13	76.5	-		5	50	2	28.5	11	84.6	59	42.5
Febrile aplasia	18	25	-		-		1	5.9	2	25	-		-		-		21	15.1
Coma	3	4.2	-		-		-		-		-		1	14.3	-		4	2.9
Organ failure [1]	3	4.2	-		-		-		1	12.5	1	10	1	14.3	-		6	4.3
Multi-Organ failure	1	1.4	-		-		-		-		-		-		-		1	0.7
Metabolic disorders [2]	10	13.9	-		-		-		-		-		1	14.3	-		11	7.9
Respiratory distress	3	4.2	-		-		-		-		3	30	-		1	7.7	7	5
Thromboembolic accident	1	1.4	-		-		-		-		-				-		1	0.7
Haemorrhage	3	4.2	1	16.7	1	16.7	-		2	25	-		1	14.3	1	7.7	9	6.5
Intracranial hypertension	1	1.4	1	16.7	-		3	17.6	-		-		1	14.3	-		6	4.3
Bowel obstruction	2	2.8	-		-		-		-		-		-		-		2	1.4
Peritonitis	1	1.4	-		-		-		-		-		-		-		1	0.7

Sepsis	2	2.8	-		1	16.7	-		2	25	1	10	-		-		6	4.3
Unknown	4	5.6	-		-		-		1	12.5	-		-				5	4
Treatment-related death	34	47.2	2	33.3	-		1	5.9	3	37.5	1	10	-		-		41	29.5
No treatment-related death	38	52.8	4	66.7	6	100	16	94.1	5	62.5	9	90	7	100	13	100	98	70.5
Note: * Gliomas (1), teratoma (1), germ cell tumor (3), hepatoblastoma (1), melanoma (1); 1. Acute renal failure (4), hepatic failure (1), respiratory failure (1); 2. Tumor lysis syndrome (6), dehydration (3), hypoglycemia (2)																		

Table 4: Distribution of causes of death with various malignancies.

Gateways identified for febrile aplasia and non-neutropenic sepsis were pulmonary (5 cases) and gastrointestinal (7 cases).

Discussion

This study revealed high death rate and high proportion of non-treatment related deaths. Cancers have a poor prognosis in Sub-Saharan Africa. Death rates in children in hospitals range from 39% to 59%, compared to populations of 690 and 88 cases respectively [5,8,9]. Most of the published studies on cancer mortality in middle and high-income countries are from clinical trials, or focus on specific cancer mortality rather than inpatient mortality as a useful epidemiological parameter [10]. Marwaha, et al. reported a 24% mortality rate in a population of 532 children with acute lymphoblastic leukemia in a center in northern India [11].

Tsurusawa, et al. in Japan found 6 deaths among 321 children treated for non-Hodgkin's B lymphoma [12].

Delayed diagnosis and advanced stages may justify high mortality rates in Sub-Saharan Africa. Indeed Weaver et al showed that in Kenya, where the average diagnostic delay was 6.8 months, retinoblastoma mortality was 73%, more than 50 times higher than the reported death rate in Canada [13]. Approximately 50-75% of children diagnosed with retinoblastoma in Africa die because of advanced stages, compared to less than 5% of deaths in developed countries where the diagnosis is early and the access to a competent team rapid [13]. The median time to diagnosis was 90 days, and 38.1% of the patients were metastatic at diagnosis in this study. Eke and Akani found a median consultation time of 8 weeks and 60% of metastatic patients [9]. 71.4% of children were metastatic at diagnosis in the Brown et al. study in the Department of Pediatrics, University College Hospital, and Ibadan, Nigeria [5].

Treatment-related deaths accounted for 29.5% and non-treatment-related for 70.5% including 42.5% due to tumor progression in this study. Concurrently O'Brien, et al. found 77% of non-treatment-related deaths, 57% of which were due to tumor progression [14]. In contrast, Prakash, in India found 71% of treatment-related deaths and 25% of deaths due to tumor progression [10]. These differences could be explained by different practices of patient care and registration of deaths, but also by the definition of death patterns used in the above studies. While tumor progression is the leading cause of death in our study, the high probability of underestimation of this cause must be emphasized. The causes identified were those mentioned in the medical file, but there was a similarity between the clinical elements considered as a tumor progression and the clinical presentations of the other non-treatment causes in several deaths. In another study conducted on a pediatric population, Brown, et al. found 27% of treatment-related deaths, and infections accounted for the leading cause of death with 39.6% [5].

Childhood studies of chemotherapy-related deaths in leukemia clinical trials in high-income countries yielded death rates ranging from 3% to 51%, and infections were the dominant causes ranging from 33% to 73% [15-19].

The weaknesses of this audit are that 44% of the deaths were not included in the study because they lacked sufficient information to be attributed to treatment-related deaths or not and to cause, most of which occurred at home. However, this work is a contribution to the study of childhood cancer mortality in Sub-Saharan Africa.

Conclusion

This study has made it possible to establish the mortality profile of childhood cancers in our department. Most deaths are due to cancer. Actions promoting early diagnosis and rapid access to treatment will reduce the mortality rate.

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